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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	10

DATE MAILED: 09/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/829,124	Applicant(s) WEI ET AL.	
	Examiner Anne Kublik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-89* is/are pending in the application.

4a) Of the above claim(s) *19-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *06/18/25* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-18) in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the claims are all closely related and would thus require common areas of search and consideration. This is not found persuasive because a search on a method of applying a protein of a particular size, for example, requires a different search than that required, for example, for a nucleic acid of a particular sequence - the former does not require a search of the nucleic acid databases and the latter does not require a search for isolated proteins. Proteins can be isolated from their natural source and characterized in detail without knowledge of the DNA that encodes them, and in fact, many proteins were isolated years before DNA cloning and sequencing were possible.

The requirement is still deemed proper and is therefore made FINAL. Claims 19-89 are withdrawn from consideration as being drawn to non-elected inventions. Claims 1-18 are examined.

2. The draftsman has approved the drawings as submitted.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the serial number of the application in the claim for benefit under 35 USC 120 is recited as "09/412,451" when it should be "09/412,452."

4. The information disclosure statement filed 15 January, 2002, fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because not all reference citations are complete. Those citations have been crossed out, and the references are not considered. Applicant is advised that the date of any re-submission of any item of information contained in

this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Objections

5. Claims 13 and 16 are objected to because of the following informalities:

In claim 13, line 4, "sprout" should be plural and "turnip" is repeated twice.

In claim 16, line 4, "sprout" should be plural and in lines 4-5 "turnip" is repeated twice.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that encode *Xanthomonas campestris* hypersensitive response elicitors of 13-15 kDa, including a multitude of nucleic acids that hybridize under low stringency conditions to SEQ ID NO:1, and plants transformed with those nucleic acids. In contrast, the specification only describes a coding sequence from *Xanthomonas campestris* pv *pelargonii* that comprises SEQ ID NO:1. Applicant

does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode a *Xanthomonas campestris* hypersensitive response elicitors of 13-15 kDa within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

8. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding a hypersensitive response elicitor of SEQ ID

NO:2, and plants transformed with that nucleic acid, does not reasonably provide enablement for any nucleic acid encoding any *Xanthomonas campestris* hypersensitive response elicitor of 13-15 kDa, and plants transformed with those nucleic acids and methods of imparting disease resistance in plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acids encoding any *Xanthomonas campestris* hypersensitive response (HR) elicitor of 13-15 kDa, including a multitude of nucleic acids that hybridize under low stringency conditions to SEQ ID NO:1, and plants transformed with those nucleic acids.

The instant specification, however, only provides guidance for growing *Xanthomonas campestris* pv *pelargonii* (*Xcp*) in culture and preparation of supernatants from the cells to produce a cell-free elicitor preparation (CFEP) (example 1); infiltration of the CFEP on a number of plants to show it induced a hypersensitive response on some species but not others (example 2); protease inactivation of the CFEP and infiltration on tobacco to show the HR elicitor is protein (example 3); chromatographic purification of the HR elicitor from the CFEP (example 4); SDS-PAGE of the purified protein (example 5); amino acid sequencing of a 9 amino acid peptide of the protein (example 6); topical treatment of tobacco plants with the protein to show that it reduced tobacco mosaic virus induced lesions in the plants (example 7) and enhanced growth of the plants (example 8); construction of an *Xcp* genomic library (example 9); probing the library with an oligonucleotide based on the amino acid sequence above and isolation of clones (example 10-11); Southern analysis of digestion fragments of those clones to identify a fragment that the probe hybridized with (example 12); subcloning that fragment (example 13);

sequencing the subclone to identify the *hreX* gene, SEQ ID NO:1, which encodes SEQ ID NO:2 (example 14); construction of an expression vector containing the *hreX* gene (example 15); transformation of the vector into *E. coli*, and infiltration of CFEP from the bacteria onto tobacco to show that it induced HR (example 16); and Southern blotting of other *Xanthomonas* species and other bacteria with the *hreX* gene to show that something hybridizes to the gene in a number of *Xanthomonas* species (example 17).

The instant specification fails to provide guidance for nucleic acids other than SEQ ID NO:1 that encode a *Xanthomonas campestris* hypersensitive response elicitor of 13-15 kDa, or for exact hybridization or amplification conditions and probes/primers to use in isolation of those nucleic acids. The instant specification also fails to provide guidance for a plant of any species that is transformed with SEQ ID NO:1 or any other nucleic acid encoding a *Xanthomonas campestris* hypersensitive response elicitor of 13-15 kDa or for ornamental plant cuttings that are resistant to desiccation.

Making "conservative" substitutions in a nucleic acid (*e.g.*, substituting one polar amino acid codon for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The nucleic acids encoding all

these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

As constitutive elicitor production can be lethal to a plant, producing disease resistance via transformation with a gene encoding an elicitor protein also requires a pathogen-induced promoter (Keller et al, 1999, Plant Cell 11:223-235, see pg 224, left column paragraph 1). The instant specification fails to teach such promoters or how lethality can be prevented without them.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate 13-15 kDa *Xanthomonas campestris* hypersensitive response elicitor-encoding nucleic acids, including those that hybridize to SEQ ID NO:1 under low stringency conditions. Making all possible single amino acid substitutions in an 114 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{114} nucleic acids. Because nucleic acids that hybridize to SEQ ID NO:1 under low stringency conditions would encode proteins with many amino acid substitutions, many more than 19^{114} nucleic acids would need to be made and analyzed.

As the specification does not describe the transformation of any plant with a gene encoding a *Xanthomonas campestris* hypersensitive response elicitor of 13-15 kDa, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with desiccation resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2-6, 8, 11 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 2 and 5 are indefinite in their recitation of the hybridization conditions because the hybridization time and the wash conditions (salt concentration, temperature and time) are not indicated.

Claims 2 and 3 are indefinite in their recitation of "an amino acid of SEQ ID NO:2". As written, the claims are drawn to a DNA molecule that encodes a protein that comprises one amino acid of SEQ ID NO:2. If this is not what Applicant intended, it is suggested that "an amino acid" be deleted.

Claims 4 and 5 are indefinite in their recitation of 'a nucleotide sequence of SEQ ID NO:1". As written, the claim is drawn to a DNA molecule that comprises a nucleotide sequence (*e.g.*, any dinucleotide) of SEQ ID NO:1. If this is not what Applicant intended, it is suggested that "a nucleotide sequence of" be deleted.

Claim 8 is indefinite for its recitation of "correct reading frame". It is not clear which reading frame is the correct one.

In claim 11, it is not clear if the DNA molecule is located on an expression vector or if the DNA molecule was cotransformed with an expression vector (of unknown properties) into the cell.

Claim 18 is indefinite in its recitation of "ornamental plant". Plants that are considered ornamental by one person may not be so considered by another. Thus, the metes and bounds of the claim are unclear.

11. Claims 1-18 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a *Xanthomonas campestris* hypersensitive response elicitor of 13-15 kDa, including SEQ ID NO:1.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Sonya Williams, at (703) 305-2272.

Anne R. Kubelik, Ph.D.
September 3, 2002

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